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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/053,410 | 11/07/2001 | Rudolf Jung | 1276 | 4333 |
| 27310 | 7590 | 01/30/2004 | EXAMINER | |
| PIONEER HI-BRED INTERNATIONAL INC. 7100 N.W. 62ND AVENUE P.O. BOX 1000 JOHNSTON, IA 50131 | | | BAUM, STUART F | |
| | | ART UNIT | | PAPER NUMBER |
| | | | | 1638 |

DATE MAILED: 01/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) |
|------------------------------|------------------------|---------------------|
| | 10/053,410 | JUNG ET AL. |
| Examiner | Art Unit | |
| Stuart F. Baum | 1638 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 30 September 2003.

2a) This action is **FINAL**. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 1-79 is/are pending in the application.
4a) Of the above claim(s) 6,17 and 21-79 is/are withdrawn from consideration.
5) Claim(s) _____ is/are allowed.
6) Claim(s) 1,2,5,7-13,16 and 18-20 is/are rejected.
7) Claim(s) 3,4,14 and 15 is/are objected to.
8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.

 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) All b) Some * c) None of:
1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.

13) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) The translation of the foreign language provisional application has been received.

14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) Notice of References Cited (PTO-892) 4) Interview Summary (PTO-413) Paper No(s). ____ .
2) Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) Notice of Informal Patent Application (PTO-152)
3) Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4/1/2002 . 6) Other: ____ .

DETAILED ACTION

1. Claims 1-79 are pending.
2. Applicant's election of Group I, claims 1-5, 7-16, and 18-20 including SEQ ID NO:3 encoding SEQ ID NO:4 filed 9/30/2003 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 6, 17, and 21-79 have been withdrawn from consideration because the claims are drawn to non-elected inventions.

3. Claims 1-5, 7-16, and 18-20 are examined in the present office action.

Claim Objections

4. Claims 1-5, 10, 13-16, and 18 are objected to for reading on non-elected inventions. Correction is required.

Claim 1, line 11 is objected to for not reciting "and" after "(c);".

Claim 10, line 13 is objected to for not reciting "and" after "(c);".

Claim 13, line 3, is objected to for not reciting "sequence" after the recitation "nucleotide".

Claim 18, line 13 is objected to for not reciting "and" after "(c);".

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-2, 5, 7-13, 16, 18-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The rejection includes dependent claims.

Claim 1 is indefinite in the recitation “a nucleotide sequence encoding a polypeptide having at least about 80% sequence identity to the nucleotide sequence”. It is not clear if Applicant is claiming a nucleotide sequence exhibiting at least about 80% sequence identity compared to another nucleotide sequence, or Applicant is claiming a nucleotide sequence encoding a protein that exhibits at least about 80% sequence identity to another protein sequence, or Applicant is claiming a nucleotide sequence encoding a protein exhibiting at least about 80% sequence identity to a nucleotide sequence. For purposes of compact prosecution, the Office interprets Applicants’ claim to mean a nucleotide sequence exhibiting at least about 80% sequence identity compared to another nucleotide sequence. All subsequent recitations of “a nucleotide sequence encoding a polypeptide having at least about 80% sequence identity to the nucleotide sequence” are also rejected. It is recommended that “having” be amended to recite -- wherein said nucleotide sequence has--.

The term “stringent conditions” in claims 1, 5, 10, 16, and 18 is indefinite because “stringent” is a relative term. The term “stringent conditions” is not explicitly defined by the claim, or the specification. Applicants only give exemplary conditions to define “stringent conditions (page 10, last paragraph). One of ordinary skill in the art would not be reasonably apprised of the scope of the invention given the indefiniteness of “stringent conditions” as defined by Applicant.

Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-2, 5, 7-13, 16, and 18-20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to an isolated nucleic acid molecule, transformed plant, or transformed plant cell, comprising a nucleotide sequence exhibiting at least 80% sequence identity with SEQ ID NO:3; an isolated nucleic acid molecule comprising a nucleotide sequence that hybridizes to SEQ ID NO:3, a nucleotide sequence exhibiting at least 80% sequence identity with SEQ ID NO:3 or a nucleotide sequence encoding SEQ ID NO:4; or expression cassette comprising a nucleotide sequence exhibiting at least 80% sequence identity with SEQ ID NO:3.

Applicants disclose an 18 kD α -globulin full-length cDNA of SEQ ID NO:3 that was isolated from maize, which encodes SEQ ID NO:4 (page 52, Example 5).

Applicants do not describe any polynucleotide sequences that hybridize to SEQ ID NO:3 or any sequences that exhibit at least 80% sequence identity to SEQ ID NO:3 and encode an 18 kD α -globulin protein.

The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of biotechnology. The court stated that, "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of

cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus.” *See University of California v. Eli Lilly and Co.*, 119 F.3d 1559; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). Applicants fail to describe a representative number of polynucleotide sequences encoding an 18 kD α -globulin protein falling within the scope of the claimed genus of polynucleotides which hybridize to SEQ ID NO:3 or sequences that exhibit at least 80% sequence identity to SEQ ID NO:3 and encode an 18 kD α -globulin protein. Applicants only describe a single cDNA and amino acid sequence of SEQ ID NO:3 and 4, respectively. Furthermore, Applicants fail to describe structural features common to members of the claimed genus of polynucleotides. Hence, Applicants fail to meet either prong of the two-prong test set forth by *Eli Lilly*. Furthermore, given the lack of description of the necessary elements essential for 18 kD α -globulin protein activity, it remains unclear what features identify an 18 kD α -globulin encoding polynucleotide. Since the genus of 18 kD α -globulin encoding polynucleotides has not been described by specific structural features, the specification fails to provide an adequate written description to support the breadth of the claims.

In addition, sequences that hybridize with SEQ ID NO:3 or sequences that exhibit at least 80% sequence identity to SEQ ID NO:3 and encode an 18 kD α -globulin protein encompass naturally occurring allelic variants, mutants of 18 kD α -globulin protein, as well as sequences encoding proteins having no known 18 kD α -globulin function, of which Applicant is not in possession. Accordingly, the specification fails to provide an adequate written description to support the genus of polynucleotides encompassed by the hybridization language or percent

identity language as set forth in the claims. (See Written Description guidelines published in Federal Register/Vol. 66, No.4/Friday, January 5, 2001/Notices: p.1099-1111).

Scope of Enablement

7. Claims 1-2, 5, 7-13, 16, and 18-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for claims drawn to the isolated nucleic acid molecule of SEQ ID NO:3 encoding SEQ ID NO:4, as well as expression cassettes, plants, plant cells and seed comprising said nucleic acid molecule, does not reasonably provide enablement for claims drawn to an isolated nucleic acid molecule, comprising any nucleotide sequence exhibiting at least 80% sequence identity with SEQ ID NO:3; any isolated nucleic acid molecule comprising a nucleotide sequence that hybridizes to SEQ ID NO:3; or expression cassette comprising a nucleotide sequence exhibiting at least 80% sequence identity with SEQ ID NO:3 or nucleotide sequence that hybridizes to SEQ ID NO:3 or a sequence that encodes SEQ ID NO:4 , or plant, plant cell or seed transformed therewith. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claimed invention is not supported by an enabling disclosure taking into account the *Wands* factors. *In re Wands*, 858/F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior

art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

The claims are broadly drawn to any isolated nucleic acid molecule, transformed plant, or transformed plant cell, comprising a nucleotide sequence of SEQ ID NO:3 or a nucleotide sequence exhibiting at least 80% sequence identity with SEQ ID NO:3; an isolated nucleic acid molecule comprising a nucleotide sequence that hybridizes to SEQ ID NO:3 or a sequence that encodes SEQ ID NO:4, or a nucleotide sequence exhibiting at least 80% sequence identity with SEQ ID NO:3; or expression cassette comprising a nucleotide sequence exhibiting at least 80% sequence identity with SEQ ID NO:3.

Applicants teach the cloning of an 18 kD α -globulin cDNA (B73 allele) from maize endosperm library (page 52, 1st paragraph). Applicants disclose transforming a maize plant with the maize 18 kD α -globulin cDNA of SEQ ID NO:3 operably linked to a gamma-zein promoter which expresses in the endosperm (page 53, 1st full paragraph) yielded plants with increased levels of 18 kD α -globulin protein and that had increased nutrition and digestibility (page 53, last full paragraph, and paragraph bridging pages 53 and 54).

Applicants do not teach nucleic acid molecules that hybridize with or have 80% identity to SEQ ID NO:3 and Applicants do not teach transforming maize or any plant with any such molecules. In addition, Applicants do not teach one skilled in the art how to use a plant transformed with a sequence that exhibits less than 100% sequence identity with SEQ ID NO:3.

The state-of-the-art is such that one of skill in the art cannot predict which nucleic acids that hybridize with or have 80% identity to SEQ ID NO:3 will encode a protein with the same activity as a protein encoded by SEQ ID NO: 3. The prediction of protein structure from

sequence data and, in turn, utilizing predicted structural determinations to ascertain functional aspects of the protein, is extremely complex, and the positions within the protein's sequence where amino acid substitutions can be made with a reasonable expectation of maintaining function are limited (Bowie et al, Science 247:1306-1310, 1990, see especially page 1306). Proteins may be sensitive to alterations in even a single amino acid in a sequence. For example, the replacement of a glycine residue located within the START domain of either the PHABULOSA or PHAVOLUTA protein receptor with either an alanine or aspartic acid residue, alters the sterol/lipid binding domain (McConnell et al, Nature 411 (6838):709-713, 2001, see especially page 710, left column, 2nd paragraph).

The state-of-the-art teaches isolating DNA fragments using stringent hybridization conditions, does not always select for the desired DNA fragments. Fourgoux-Nicol et al (1999, Plant Molecular Biology 40 :857-872) teach the isolation of a 674bp fragment using a 497bp probe incorporating stringent hybridization conditions comprising three consecutive 30 minute rinses in 2X, 1X and 0.1X SSC with 0.1% SDS at 65⁰C (page 859, left column, 2nd paragraph). Fourgoux-Nicol et al also teach that the probe and isolated DNA fragment exhibited a number of sequence differences comprising a 99bp insertion within the probe and a single nucleotide gap, while the DNA fragment contained 2 single nucleotide gaps and together the fragments contained 27 nucleotide mismatches. Taking into account the insertions, gaps and mismatches, the longest stretch of contiguous nucleotides to which their probe could hybridize consisted of 93bp of DNA (page 862, Figure 2). In the present example taught by Fourgoux-Nicol et al, the isolated fragment exhibits less than 50% sequence identity with the probe.

The state-of-the-art of isolating or synthesizing nucleic acid molecules that encode a polypeptide of defined function is highly unpredictable. Applicants do not teach which amino acids of SEQ ID NO:4 can be deleted or substituted and still produce a protein that improves nutrition and digestibility of corn seeds. It cannot be predicted by one of skill in the art that nucleic acids that hybridize to SEQ ID NO:3 or sequences that exhibit 80% sequence identity with SEQ ID NO:3 will encode a protein that improves nutrition and digestibility of corn seeds as the polypeptide of SEQ ID NO: 4.

In view of the lack of guidance, undue trial and error experimentation would be required for one of ordinary skill in the art to screen through the multitude of non-exemplified sequences, either by using non-disclosed fragments of SEQ ID NO:3 as probes or by designing primers to undisclosed regions of SEQ ID NO:3 and isolating or amplifying fragments, subcloning the fragments, producing expression vectors and transforming plants therewith, and then to evaluate each plant for a desirable phenotype or characteristic.

Therefore, given the breadth of the claims; the lack of guidance and examples; the unpredictability in the art; and the state-of-the-art as discussed above, undue experimentation would be required to practice the claimed invention, and therefore the invention is not enabled throughout the full scope of the claims.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

8. Claim 19 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claim 19 is drawn to a seed of the transformed plant. Due to Mendelian inheritance of genes, a single gene introduced into a parent plant would only be transferred at most to half the male gametes and half the female gametes. This translates into only three quarters of the progeny having at least a single copy of the transgene and one quarter of the progeny would not carry a copy of the transgene. Given that there is no indication that there would be any other distinguishable characteristics of the claimed progeny (seeds), it is unclear whether the claimed seeds would be distinguishable from seeds that would occur in nature. See *Diamond v. Chakrabarty*, 447 U.S. 303 (1980), *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 76 USPQ 280 (1948), and *In re Bergy, Coats, and Malik* 195 USPQ 344, (CCPA) 1977. The amendment of the claims to recite that the seeds comprise the construct that was introduced into the parent seed would overcome the rejection.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1 and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Shorrosh et al (1999, NCBI Accession number X63990).

The claims are drawn to an isolated nucleic acid sequence that hybridizes under stringent condition to SEQ ID NO:3.

Shorrosh et al teach a nucleic acid sequence that exhibits 18% sequence identity to SEQ ID NO:3 and hybridizes to SEQ ID NO:3. Because of the 112 2nd indefiniteness of “stringent conditions” as discussed above, the Office interprets the phrase to encompass any hybridization conditions. Hence, the sequence disclosed by Shorrosh et al anticipates the claimed invention.

10. Claims 1, 7, 10-12, 16, and 18-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Singh et al (1997, Plant Science 130:189-196).

The claims are drawn to an isolated nucleic acid molecule, expression cassette, transformed rice plant or seeds comprising a nucleotide sequence that hybridizes under stringent conditions to a nucleotide sequence that exhibits at least 80% sequence identity to SEQ ID NO:3.

Singh et al teach a rice plant transformed with a legumin seed storage protein. Because of the 112 2nd indefiniteness of “stringent conditions” as discussed above, the Office interprets the phrase to encompass any hybridization conditions, and as such, the sequence of Singh et al hybridizes to a sequence exhibiting at least 80% sequence identity to SEQ ID NO:3, or hybridizes to SEQ ID NO:3. It would be an inherent component of the system to generate seeds, and as such, Singh et al anticipate the claimed invention.

11. Claims 2-4, 8-9, 13-15, and 20 are deemed free of the prior art, given the failure of the prior art to teach or reasonably suggest an isolated nucleic acid, expression cassette, transformed plant or plant cell comprising a nucleotide sequence exhibiting at least 80% sequence identity to

SEQ ID NO:3, or a sequence set forth in SEQ ID NO:3 or encoding an amino acid sequence set forth in SEQ ID NO:4.

12. Claims 3-4, and 14-15 are objected to but would be allowable if rewritten to overcome the objections as stated above.

13. Claims 1-2, 5, 7-13, 16, and 18-20 are rejected.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart F. Baum whose telephone number is 571-272-0792. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on 571-272-0804. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Stuart F. Baum Ph.D.

January 23, 2004



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SUPERVISORY PATENT EXAMINER
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